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REVIEW ARTICLE

Paederia foetida - a promising ethno-medicinal tribal plant of north-eastern India

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Abstract: The northeastern region of India constitutes one of the biodiversity hotspots of the world. The ethnic groups inhabiting this region practice their distinctive traditional knowledge systems using biodiversity for food, shelter and healthcare. Among the less-studied plants, *Paederia foetida* has been used by various ethnic tribes as food and medicine. Many of its therapeutic properties relate to the gastrointestinal system and suggest its potential utility for gastrointestinal ailments. This is a review of the ethnobotanical uses, phytochemistry and therapeutic properties of *P. foetida* compiled from various reports. *P. foetida* is promising as a remedy for life-style related conditions, especially treatment of ulcers. Its utility highlights the need for proper evaluation of tribal plants as medicines and the species could be considered for development of new drugs.

Keywords: *Paederia foetida*; Tribal medicine; ethnobotany; phytochemistry; therapeutic; ulcer

Introduction

The Northeastern (NE) region of India, approximately of 263,179 km^2, is part of the Himalayan and Indo-Burmese biodiversity hotspots. Its unique biogeography comprises of major biome types such as grassland, swamp, marsh and forest (evergreen, deciduous, scrub and alpine). The region has attracted attention for its indigenous cultures, traditions, heritage and food habits. In this context, it is necessary to consider the neglected or little known species used by the tribal of NE as food and medicine. The wild varieties of many cultivated crops are considered to have originated in this region. Supporting around 50% of India's biodiversity, this area is also home to more than 200 tribes of different ethnicities with unique customs. These tribes have distinctive traditional knowledge systems based on use of biodiversity for food, shelter and healthcare (Mao et al. 2009). Many ethno-botanical studies have documented names and applications of plant species used by the people of this region. However, these studies typically list the species names and uses only. Since most of these plants are indigenous to this region and the knowledge base remains within the ethnic groups, there is a lack of awareness of these plants, accurate methods of preparation, edible and/or medicinal uses and their active principles. It has been postulated that this traditional knowledge of system and biocultural diversity are interdependent aspects amongst these societies and are necessary for community development (Braton 1989; Agrawal and Gibson 1999).

In the case of wild edible plants, nutritional information is also to be documented. Most of these indigenous plants are not cultivated. Some of them (such as *Panax assamicus*, *Paris polyphylla*, *Dendrobium denudans*) face demands from other countries and drug companies, or are harvested unsustainably from the wild due to socio-political changes, ineffective harvest management, lack of arable land, and other pressures (Swiderska 2006; Pilgrim et al. 2007; Turner and Turner 2007; Singh et al. 2009). These practices have led to many plant species being formally listed as threatened.

There is a need for prioritization of research on the wild plants with detailed studies on active principles and nutritional components. An estimated 1600 plant species are used in Indian traditional systems of medicine, of which more than 80% are used in ethnomedicine in northeast India alone, indicating the rich traditional knowledge systems of northeast India. The rich knowledge, art and system of tribal medicine, if studied scientifically, might

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yield benefits not only to medicinal prevention and cure but also to understanding of the nutritional importance and value of the wild products used as food. Among the lesser studied wild plants, *P. foetida* L. or skunk vine in English (syn. *Paederia chinensis* Hance, *Paederia scandans* (Lour.) Merr, *Paederia tomentosa* Blume) (Global Invasive Species Database 2012), is used by many ethnic tribal groups as food and medicine (Fig. 1a, b & c). Belonging to family Rubiaceae, it is a climber found to elevations of around 1800 m and is also found in Bihar, Orissa, Bengal and Assam (Nadkarni 1982). The main parts used are leaf, root, bark and fruit. Several reports document the dual use of the wild plant as food and medicine (Dutta and Dutta 2005; Jamir et al. 2010; Jasmine 2007; Kagyung et al. 2010; Kar and Borthukar 2008a; Kayang 2007). Of nine vegetation types in India, six important vegetation types are found in the northeast region. This richness of biological resources encourages researchers from university, government and private institutes to explore this region for wild plants (Chakraborty et al. 2012; Mao et al. 2009). A unique characteristic of this plant is the foetid smell produced when the leaf is mechanically ruptured.

Fig. 1 Whole plant (a), dried stem (b) and dried seed (c) of *P. foetida* L.

Phytochemistry

P. foetida produces compounds that are responsible for its diverse uses. The aerial parts of the plant contain iridoid glycosides which are optically active cyclopentanoid monoterpenes. These are one of the most important defensive secondary metabolites produced by the plant. The iridoid glycosides (Shukla et al. 1976) produced by *P. foetida* are paederoside (0.084%), asperuloside (0.08%) and scandoside (0.064%). Paederoside is a monoterpene S-methyl thiocarbonate (Kapadia et al. 1979). An enzyme splits paederoside to sulphur containing methyl-mercaptan and it is released when the plant tissues are ruptured. The ill smelling principle of *P. foetida* is due to methyl mercaptan (Anonymous 2001; Bose et al. 1955; Chopra et al. 1969). Studies reveal the diverse activity of iridoid glycoside viz. anti-oxidant, anti-bacterial, anti-nociceptive, analgesic, anti-inflammatory, diabetic, and hepatoprotective. The plant also contains alkaloids paederine a and b and essential oil (Samy et al. 2005). Different types of volatile compounds are also isolated by steam distillation from the leaves and stems of which linalool is the major component. There is a high percentage of mineral elements in the plants. Nitrogen, phosphorus, potassium and magnesium are major constituents in comparison to calcium, zinc copper and manganese (Upadhyaya et al. 2010). The other major constituents present in the plant are ursolic acid, β-sitosterol, oleanolic acid, arachidic acid. It has been postulated that presence of these triterpenoids (ursolic acid, oleanolic acid and their derivatives), saturated fatty acid (arachidic acid) and β-sitosterol may be responsible for its anti-ulcer activity (Das 1998; Liu 1995; Onasanwo et al. 2010). Table 1 lists the isolated phytoconstituents.

Traditional/Folkloric uses in food and medicine

Traditionally the tribal people of NE administer the plant in different form according to their need/ailments. For medicinal purpose, decoction of the whole plant, leaf, stem, stem bark, or leaf juice is prepared. Tender leaves are boiled and eaten with chili and salt as food. Tribes of Tripura state prepare 'Berma batui or Gudak' using dry fish and leaves of *P. foetida* (Das 1997). Tribal people of Chittagong hill tracts of Bangladesh and the Aka tribe of Arunachal Pradesh consume the leaf juice to treat diarrhoea, dysentery and burns or scalding. It has also been reported that the powder form of the whole plant is taken by certain tribal communities in other parts of India for weakness and rheumatic joint pains. Certain ethnic communities of Orissa state of India cook the leaves with rice to cure different joint diseases like rheumatism and gout (Singh et al. 2010). Fresh leaves are available in the Calcutta local markets and the patients, particularly those suffering from bowel complaints, use these in soups and in other food preparations. It is also used by invalids and convalescents (Anonymous 2001). Adi and Memba tribes of Arunachal Pradesh use leaves and twigs as vegetables eaten with rice (Kagyung et al. 2010). *P. foetida* is a wild food for the tribal people of Andhra

Pradesh, who use the leaves as vegetables (Reddy et al. 2007). Presence of high amounts of protein (5%), fat (1%), carbohydrate (3%), dietary fiber, minerals (nitrogen, phosphorus, potassium, natrium, iron, magnesium, calcium, zinc, copper, and manganese), vitamin C, and phenolic content increase its nutritional and medicinal values. Srianta et al. (2012) reported the presence of Vitamin C (271 mg per 100 g) and phenolics in leaves, indicating their anti-oxidant properties. *P. foetida* is also indexed as a vegetable drug in Basavarajeeyam, an important Ayurvedic text in the Andra region (Raju 2001). Traditional uses of *P. foetida* are tabulated in Table 2.

Table 1. Isolated phytoconstituents from *P. foetida*

Isolated constituents	Plant part(s)	Reference
Iridoid glucoside; asperuloside(0.08%); scandoside(0.064%); paederoside(0.084%)	Aerial part	Shukla et al. 1976
Alkaloids; Paederine a; Paederine b	Leaf, stem	Samy et al. 2005
Essential oil; Monoterpene- major Linalool; methyl mercaptan. Tepineol, geraniol, 2-methyl 3-ethylmaleic anhydride	Leaf, stem & flower	Samy et al. 2005 Wong and Tan 1994
Hentiracontane; hentriacontane; ceryl alc; hentriacontanol; palmitate; sitosterol; stigmasterol; campesterol; ursolic acid; 2,3-dihydrobenzofuran; benzofuran and sulphur containging compounds dimethyl sulphide and dimethyl trisulphide, epifriedelinol, friedelin; Embelin	Leaf, stem Aerial part	Shukla et al. 1976
Vitamin C	Leaf	Nosalova et al. 2007
Nonanoic acid; capric acid; lauric acid; myristic acid; arachidic acid;, palmitic acid; conjugated dienoic acid and trieonic acid	Leaf	De et al. 1993a
Saurated hydrocarbon; Friedelan-3-one and β-sitosterol;epifriedelanol (I),	Whole plant	Tripathi & Dasgupta 1974; Ahmed et al. 1991

Table 2. Traditional/Folkloric uses of *P. foetida.*

Plant part used	Location (State/Country)	Traditional uses
Leaf	India	Tonic, astringent, Convalescents, in bowel complaints, in rheumatism, abdominal distension, flatulence, herpes (Anonymous 2001).
	Assam	Allergy (Kalita & Deb 2006), in gastralgia, post natal pain and bleeding (Purkayastha & Nath 2006) diarrhoea and dysentery (Barua et al. 2007; Borah et al. 2006; Basumatary et al. 2004; Kar & Borthakur 2008a, b), as vegetables (Barua et al. 2007), abdominal pain (Kalita & Phukan 2010).
	Tripura	As vegetable, diuretic, in diarrhoea, infection (Das 1997; Chanda et al. 2011).
	Andhra Pradesh	As vegetable (Reddy et al. 2007)
	Arunachal Pradesh	Urinary disorder, kidney stone and digestive problem (Sarmah et al. 2008) also with rice as vegetables in indigestion (Kagyung et al. 2010), in gastric trouble, to clean stomach and against stomach swelling and diarrhoea (Srivastava & Singh 2010), gastritis and loose motion (Tangjang et al. 2011).
	Sikkim and Darjeeling	Anti diabetic (Chhetri et al. 2005)
	Meghalaya; Orissa	As anti dote for snake bite (Hynniewta & Kumar 2008); Rheumatism and gout (Singh et al. 2010).
	Philippine	Applied to abdomen in case of retention of urine; as diuretic and to dissolve vesicle calculi (Anonymous 2001).
	Bangladesh	Diarrhoea, to relieve distention and flatulence (Chopra et al. 1969).
Root	India	Emetic, piles, inflammation of spleen, pain in chest and liver, (Anonymous 2001); Asthma, seminal weakness (Chopra et al. 1969).
Bark	Philippine	Emetic (Anonymous 2001)
Fruit	Philippine	Toothache (Anonymous 2001)

Therapeutic properties and mechanisms of action

Apart from published literature on traditional usage, *P. foetida* has been reported to have wide-ranging therapeutic properties; the possible mechanisms of action have also been indicated for some properties.

Antidiarrhoeal activity

Diarrhea is a leading cause of mortality and morbidity, especially among children in developing countries, resulting in a major health care problem. The World Health Organization (WHO)

encourages traditional medical practices for treatment and prevention of diarrheal diseases (Atta and Mouneir 2004). In India and few other parts of Asia, *P. foetida* has folkloric use as a remedy for diarrhea and dysentery (Chopra et al. 1969; Chopra et al. 1956; Barua et al. 2007; Borah et al. 2006; Kar and Borthukar 2008a,b; Kalita and Phukan 2010; Das 1997; Chanda et al. 2011; Srivastava and Singh 2010). Ethanolic extract of *P. foetida* showed anti-diarrhoeal activity by using castor oil and magnesium sulphate-induced diarrhoea models in mice. The mechanism behind the activity is the reduction in gastrointestinal motility and significant increase of the latent period of diarrhea. Afroz et al (2006) suggested that the extract enhanced the morphine-induced reduction of motility at a dose of 500 mg·kg^{-1} at two time intervals.

Hepatoprotective activity

Liver diseases represent a major problem with significant morbidity and mortality. According to CDC (Center for Disease Control and Prevention) the 12th most common cause of death in US adults is liver disease and cirrhosis. The Indian system of medicine utilizes many herbs for treatment of liver disease. Studies revealed the hepatoprotective activity of the methanolic extract from the leaf of *P. foetida* in carbon tetrachloride (CCl_4) induced chronic hepatotoxicity in rats. The extract significantly decreased the elevated level of glutamate-oxaloacetate transaminase (GOT), glumate-pyruvate aminotransferase (GPT), and total protein at the dosage of 100 and 200 mg·kg^{-1} body weight (b.w.) of rat. Uddin et al. (2011) reported on the protection mechanism of the plant against hepatotoxin induced oxidative damage, where there was a 40% reduction in lipid peroxide levels at a dosage of 200 mg·kg^{-1} body weight. Other studies also indicate its moderate hepatoprotective activity, which could be a basis for its therapeutic application in various liver disorders (De et al. 1993b; De et al. 1996; Yang et al. 1987).

Antitussive activity

Cough is a protective reflex to remove foreign materials, secretion or microbes from the breathing passage. Antitussive agents are predominantly used for the suppression of dry and painful cough. Nosalova et al. (2007) evaluated the antitussive activity of the ethanolic extract of *P. foetida* on conscious cats by mechanical stimulation of laryngopharyngeal (LP) and tracheobronchial (TB) mucous areas of airways. The ethanolic extract at an oral dose (p.o.) of 200 mg·kg^{-1} b.w. had a cough-suppressive effect and the antitussive activity was 25.3% which was similar to non-narcotic antitussive dropropizine at the intraperitoneal (i.p.) dose of 100 mg·kg^{-1} body weight (28.3%). but less than that of the narcotic antitussive codeine (37%) at the dose of 10 mg·kg^{-1} b.w. i.p. (Nosalova et al. 2007). The Antitussive activity was suggested to be due to its anti-inflammatory mechanism.

Anti-arthritic activity

Arthritis is an inflammatory disorder mainly occurring in peripheral joints or in tissues surrounding a joint. Clinical studies have revealed that *P. foetida* was more effective in the treatment of rheumatoid arthritis than *Merremia tridentate*, a medicinal plant used in South India for such ailments. Rajashekhara et al. (2009) reported that after 42 days of clinical treatment, 65% of patients showed relief from joint pain, 70% from swelling, 75% from stiffness, and 70% from tenderness. The plant also lower elevated levels of acute phase proteins so it can be used as a disease modifying anti-rheumatic drug (DMARD) and can provide advantages over non-steroidal anti inflammatory drugs (NSAIDs) as the latter have no effect on these proteins. Independent studies confirmed the same activity of the plant on albino rats (Chaturvedi and Singh 1965; Singh 1970).

Anti-inflammatory activity

Inflammation is a disorder caused by the release of leukocytes and various other complex mediator molecules such as prostaglandins, leukotrienes, histamines, bradykinin, platelet activating factor and IL-1 from tissues and migrating cells (Prakash et al. 2009; Ravi et al. 2009). A detailed investigation on the anti-inflammatory activity of the butanol fraction of a methanolic extract of defatted leaves of *P. foetida* produced a more potent inhibition (52 % and 59% at dosages of 100 and 200 mg·kg^{-1} b.w. i.p. respectively) of granulation tissue formation in cotton-pellet implanted rats as compared to standard i.e. only 29% for phenylbutazone at a dosage of 100 mg·kg^{-1} i.p. It decreased liver aspartate transaminase activity without affecting serum aspartate transaminase activity. Studies report elevation of serum orosomucoid levels in rats by the plant extract which reflects the presence of anti-rheumatic properties in it (De et al. 1994; Singh et al. 1994). The percentage of anti-inflammatory activity of *P. foetida* was shown to be dose dependent (Srivastava et al. 1973). At two different dosages of 20.5 and 41 mg·kg^{-1} the percentages of anti-inflammatory activity were 38.55 and 48.97 respectively, which was stronger than acetylsalicylic acid (37.5% of anti-inflammatory activity at a dosage of 50 mg·kg^{-1}) but weaker than hydrocortisone (61.46% of anti-inflammatory activity at a dosage of 0.5 mgkg^{-1}).

Antioxidant activity

It has been documented in many studies that control of free radical production can reduce the onset of neurodegenerative diseases and slow the aging process (Wannang et al. 2008). Many studies have shown antioxidant activity of *P. foetida* extracts. Fresh and dried methanolic extracts of *P. foetida* were studied using β-carotene bleaching and the 2,2'-azinobis 3-ethylbenzothiazoline- 6-sulfonic acid (ABTS) radical cation assay (Osman et al. 2009; Dasgupta and De 2007). The percentage of antioxidant activity for extract of fresh samples using both assays (β-carotene & ABTS) was 78% and 75%, respectively, whereas in case of dried sample it was 66% and 67%, respectively. Antioxidant activity of the plant may be due to the presence of phenolic compounds (Rice-Evans et al. 1997; Holmes 1892; Zheng and Wang 2001) as such compounds function as

free-radical scavengers, reducing agents, and quenchers of singlet-oxygen formation (Andlauer and Furst 1998). The presence of vitamin C as one of the metabolites also could be a major reason for its antioxidant activity. Another study using DPPH assay also revealed free radical scavenging activity with an IC_{50} value of 4.53 mg·mL^{-1} (Srianta et al. 2012). The same activity was also reported by Kumar et al. (2009).

Neurodegenerative disorders

Supplementation of antioxidants for oxidative stress leads to protection from neurodegeneration. Hence *P. foetida* can be used against neurodegenerative diseases due to its anti oxidant properties (Amin and Tan 2002).

Antiproliferative / anticancer Activity

Reactive nitrogen species (RNS) and Reactive oxygen species (ROS) lead to different pathological disorders including arthritis, liver diseases, coronary diseases or even cancer, an environmental multifactorial disease, though the risk is also influenced by different genetic factors (Anand et al. 2008). As per Bangladeshi folk medicine, the plant possesses anticancer potential. In a clinical study, 50% ethanolic extract was shown to have anticancer activity against human nasopharyngeal epidermoid carcinoma in tissue culture, hence its traditional use as an anticancer agent was justified. This activity may also be due to its anti-inflammatory activity or antioxidant activities (Costa-Lotufo et al. 2005). Anti-cancer activity was also observed while testing the 50% ethanolic leaf extract on L-1210 lymphoid leukaemia in mice (Dhar et al. 1968).

Antihelminthic Activity

Data in India or other parts of Asia claim its uses mainly related to gastrointestinal disorders whether as anti-diarrheal, or anti-ulcer, in gastritis or in flatulence or even against parasitic worms. In poor developing tropical or semitropical countries about 2 billion people are infected by helminthes. Dey and Pal (2011) screened for antihelminthic activity of the methanolic leaf extract against *Pheretima posthuma* and *Tubifex tubifex* in a dose-dependent manner. *P. foetida* was 100% effective against *Strongyloides sp.*, *Trichostrongylus sp.* and *Haemonchus sp.*, and 50%−70% effective against *Bunostomum sp.*and *Monezia sp.* at a dosage of 4–10 oz. according to body weight, at two-days intervals over a week (Roychoudhury et al. 1970).

Analgesic activity

Analgesic activity was evaluated using the acetic acid induced writhing inhibition method (Hossain et al. 2006) on mice and significant antinociceptive activity was observed at a dosage of 150 mg·kg^{-1} p.o. Hexane, ethyl acetate and methanolic extract showed 21%, 9% and 19% inhibition respectively, whereas doses of 300 mgkg^{-1} showed 37%, 12% and 25% inhibition respectively. It was proposed that the ethyl acetate extract did not contain analgesic principles as compared to the hexane and methanolic extract. In the same experiment aminopyrine at 50 mg·kg^{-1} showed 63% writhing inhibition. Analgesic activity was postulated to be due to inhibition of the prostaglandin pathway.

Anti-ulcer activity

There are many scientific and traditional claims to the benefits of *P. foetida* with reference to gastrointestinal tract disorders such as diarrhoea, dysentery, loose motion, stomach swelling and cleaning, piles, abdominal pain, carminative, spasms, gastralgia, flatulence or other gastric ailments such as gastritis and ulcer (Barua et al. 2007; Borah et al. 2006; Basumatary et al. 2004; Kar and Borthukar 2008a,b; Pfoze et al. 2012; Srivastava and Singh 2010; Tangjang et al. 2011). As can be inferred from data in Table 2, different communities of tribal people from various geographic regions of India use this plant not only as a vegetable but also for ailments such as ulceration or other gastric ailments (Das 1997; Chanda et al. 2011; Reddy et al. 2007; Sarmah et al. 2008; Kagyung et al. 2010).

Miscellaneous

Shigellosis is one of the major food-borne bacterial diseases manifested by diarrhea, dysentery, vomiting and bloody mucus stool and accounts for approximately 0.011% of death in Asia (Bardhan et al. 2010). *P. foetida* has been evaluated for its use in the treatment of acute shigellosis (Haider et al. 1991).

Herbal formulation

Many herbal formulations incorporating *P. foetida* extracts are available in the market (Asad et al. 2007). The dosage recommended is 2–4 g (Anonymous 2009) while 2–6 g dried powder gave moderate relief in rheumatic patients (Anonymous 2010).

Conclusions

P. foetida is widely used as a medicinal plant but studies strongly support its use as food as well as medicine. It is one of the popular vegetables used by tribal communities of India. The plant extract is used in many polyherbal formulations especially those meant for arthritis patients. There are many scientific and traditional claims documenting the benefits of *P. foetida*, as shown by our review. *P. foetida* yields various therapeutic effects mainly concerned with gastrointestinal tract disorders including ulcer. Other therapeutic properties are hepatoprotective, anti inflammatory, antitussive, anti arthritics, antioxidant, analgesic, and others. *In vivo* and *in vitro* models provide data needed to assess its suitability for medicinal use. Many studies have documented the effectiveness of *P. foetida* with reference to lifestyle-related conditions, such as ulcer. *P. foetida* can serve as a good candidate plant for further evaluation since effective medicines are not available or where available, do not provide long-term relief.

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